

PATENT APPLICATION

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 INVENTOR(S): Rolf, David, 1948 East River Terrace, MN 55414, Minneapolis, US;
 Sjoblom Urmann, Elisabeth K., 1337 Edgcumbe Road, MN 55116, St. Paul, US
 PATENT ASSIGNEE(S): LecTec Corporation, 10701 Red Circle Drive, Minnetonka, Minnesota 55343, US
 PATENT ASSIGNEE NO: 291322
 AGENT: Neidl-Stippler & Partner, Rauchstrasse 2, D-81679 Muenchen, DE
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ABSTRACT (ENGLISH):

A non-occlusive medication patch (32) to be applied to the skin includes a porous self-supporting backing layer (10) to give the patch the required integrity and strength by acting as a supporting framework for other components, and a flexible hydrophilic pressure-sensitive **adhesive** reservoir (20) comprising a natural or synthetic polymer for the sustained release of medication to be absorbed topically through the skin into the body of a patient. The reservoir has two portions: first, an external coating layer (24) with an exposed lower skin-contacting surface (24b) that forms a pressure-sensitive bond with the skin, and second, an upper internal portion (24a) which infiltrates the porous backing (10) and becomes solidified therein after being applied so that the reservoir and the backing are unified, enabling the backing itself to act as a storage location for the medication-containing reservoir (20). The medication within the reservoir migrates over time from within the backing (10) through the lower coating layer (24b) and passes through the skin to provide sustained release of the medication into the body of a patient.

<image>

DESCRIPTION (ENGLISH):

FIELD OF THE INVENTION

This invention relates to a non-occlusive **adhesive** patch for applying medication to the skin.

SUMMARY OF THE INVENTION

A non-occlusive medication-containing **adhesive** patch is provided for being applied to the skin for releasing a medication into the body of a patient. The patch has a porous backing layer that can be formed from a fibrous material, e.g., non-woven fabric. To the backing is applied a flexible pressure-sensitive **adhesive**, typically a hydrocolloidal gel which serves as a reservoir for the sustained release of a medication which is uniformly distributed throughout the **adhesive** layer. The pressure-sensitive reservoir has two portions including, an external coating layer portion with an exposed surface for bonding to the skin and an internal portion that is infiltrated within the porous backing layer. The **adhesive** reservoir comprises a natural or synthetic polymer and a biomedically active medication dispersed therein. The internal portion of the hydrocolloidal reservoir which infiltrates the backing is solidified within the pores and interstices within the backing so that the reservoir and the backing are unified, enabling the backing itself to act as a storage location for the medication-containing reservoir. The gel reservoir is applied as a fluid. Solidification of the gel reservoir is delayed until after the gel has been applied to the porous backing layer.

THE FIGURES

Figure 1 is a perspective diagrammatic view illustrating a preferred method of forming products in accordance with the invention;

Figure 2 is a perspective view of the improved medication patch applied to the body;

Figure 3 is a plan view showing the medication patch packaged within in a pouch used as a shipping package;

Figure 4 is a cross-sectional view of the medication patch taken on line 4-4 of Fig. 3 with a portion of the liner sheet partially removed; and

Figure 5 is a greatly enlarged microscopic view of the medication patch and liner sheet taken on line 5-5 of Fig. 4.

DETAILED DESCRIPTION OF THE INVENTION

Refer now to Fig. 1 which illustrates diagrammatically the production of medication-applying patches in accordance with the invention. The backing sheet 10 is unwound continuously from a supply roll 12, passes upwardly in the figure over an idler roll 14 and then travels horizontally beneath a continuous processing mixer 16 where freshly prepared fluid hydrogel material at 20 is applied to the upper surface of the backing sheet 10.

The backing 10 is a porous self-supporting sheet of water insoluble polymeric material that provides strength and integrity for the **adhesive** patch as well as acting as a substrate for receiving and retaining a portion of the liquid hydrogel as will be described below.

One preferred backing sheet 10 is a lightweight, pliable strip composed, for example, from a nonwoven fabric which consists of polymeric fibers such as polyester, **cotton** or cellulose fibers bonded together with a sizing resin. The backing sheet 10 should be nonirritating to human skin. If desired, the backing sheet 10 can be coated on its back surface with a release coating such as a silicone release coating as described in patent 4,696,854 which is incorporated herein by reference. One suitable release coating is a 100% solids electron beam curable silicone such as Tego.reg. Resin **Acrylates**/RC-Series RC 705 and RC 726 by Goldschmidt Chemical Corporation of Hopewell, Virginia. The

preferred backing sheet 10 is a porous polymeric water insoluble nonwoven fibrous fabric. A suitable sizing material for bonding the fibers together is a latex resin.

The backing sheet 10 can comprise other stable, water insoluble flexible sheet materials. One preferred backing comprises a 0.14 mm strip of nonwoven fabric formed from a mixture of cellulose fibers derived from wood pulp and polyester fibers. The fibers are assembled loosely into the backing to maintain porosity. A unifying or sizing resin is applied to hold the fibers together. The sizing resin can comprise a nonirritating resin applied as a latex emulsion. One example is Hycar.reg. 26477, a resin produced by B.F. Goodrich Co. of Brecksville, Ohio. Another suitable backing sheet is a nonwoven fabric comprising a wetlay cellulose and polyester nonwoven fabric containing as a sizing an **acrylic** latex emulsion resin, e.g., product number N7601 by Dexter Corporation of Windsor Locks, Connecticut.

In another embodiment of the invention, the backing sheet 10 comprises a porous woven 0.12 mm acetate polymer cloth sometimes known as "silk cloth." Another form of backing sheet 10 is an open-cell plastic foam strip of low density polyethylene or polyvinyl acetate resin. Other backing sheets that can be used include woven **cotton** cloth or other cloth formed from a synthetic polymer. Suitable synthetic cloths include **nylon**, polyester, polyacetate. When the backing sheet 10 is a woven cloth, no sizing resin is needed. The backing sheet 10 is pervious to air so that the patch is non-occlusive to the skin.

The porosity of the backing sheet 10 is important because it provides openings for receiving the hydrocolloidal medication-containing reservoir and it helps to assure that the patch is non-occlusive to the skin. The infusion of the pressure-sensitive hydrocolloidal medication-containing reservoir into the backing sheet 10 is accomplished by controlling manufacturing parameters so as to keep the hydrocolloid sufficiently fluid to prenetrate the backing sheet 10 in spite of its tendency to thicken rapidly when applied. In order to prevent the consistency of the hydrogel from building too fast, i.e., becoming too viscous to properly penetrate the backing sheet 10, a continuous processing mixer 16 (Fig. 1) which includes rotating auger 18 is chilled to help remove heat produced during mixing and keep the hydrogel cool until applied to the backing 10. This can be accomplished by providing the processing mixer 16 with a cooling jacket through which a coolant such as a chilled mixture of water and ethylene glycol is passed during operation. The components of the hydrogel are continuously added to the mixer 16 during operation. While any suitable mixer 16 can be used, one suitable mixer is a 12.7 cm continuous processing mixer manufactured by Teledyne Readco Company of York, Pennsylvania. The coolant passed through the processing mixer 16 can be maintained at about 0.degree.C. The temperature of the fluid hydrogel 20 as it flows onto the exposed surface of the backing sheet 10 is important for controlling the infiltration of the coating into the backing sheet 10. The coolant will, under typical operating conditions, keep the extruded hydrogel 20 at a temperature of about 9.degree.C to 14.degree.C as it comes into contact with the backing 10. If deeper penetration is desired, the temperature of the hydrogel is lowered to about 9.degree.C for a typical hydrogel formulation. If less penetration is wanted, the temperature is raised closer to 15.degree.C.

The hydrogel produced by the processing mixer 16, which is in a chilled fluid condition, is expelled at 20 onto the exposed upper surface of the backing sheet 10 adjacent to a knife blade 22 of a knife coater which is held in spaced relationship above a rotatable support roll 23. The distance between the knife 22 and the roll 23 is controlled in any suitable manner, as by means of adjustment screws (not shown) or, if desired, the desired gap or spacing between the knife 22 and roll 23 can be preset to accommodate the backing sheet 10 and the thickness of the

hydrogel coating 24 that is being applied to the exposed surface of the backing sheet 10.

In accordance with the invention, the medication-containing hydrogel 20 is applied so as to penetrate a substantial portion of the backing sheet 10, e.g., typically between one-fourth to nine-tenths the thickness of the backing sheet 10. The penetration of the coating 24 into the backing 10 can be seen in Fig. 5. In this case the hydrogel coating 24 has penetrated about three-fourths of the way through the backing sheet 10 to provide an upper, i.e., internal layer 24a of hydrocolloidal material within the pores between the fibers making up the porous backing sheet 10. The hydrogel material thus includes two layers as seen in Fig. 5; the external coating layer 24 with an exposed pressure-sensitive surface 24b and the upper internal portion 24a which infiltrates and becomes solidified within the backing in the interstices between the fibers that make up the porous backing sheet 10.

In one product with very good characteristics the backing sheet 10 is 0.14 mm in thickness and the external part of the coating layer 24 is 0.2 mm in thickness to provide a combined thickness for the patch when applied to the body of 0.34 mm. The external hydrogel layer 24 is purposely maintained relatively thin. The hydrocolloidal **adhesive** reservoir infiltrates into the backing to a depth of about 0.05 mm to 0.13 mm to provide a total hydrocolloid layer, including both the internal and external portions, of about 0.25 mm to 0.33 mm. Because of its thickness, the medication-containing reservoir provides a very adequate supply of medication to assure sustained release of the medication over an extended period of time, e.g., six to eight hours or more. During use, the medication in the internal reservoir portion 24a stored within the backing sheet 10 migrates from within the backing sheet 10 through the external coating layer 24 and then passes through the skin to provide sustained release of the medication into the body of the patient.

After the hydrogel layer 24 is applied to the backing 10, the backing sheet continues moving toward the right as seen in Fig. 1 into close proximity with an oven or heater, in this case a radiant electric heater 25 which radiates heat onto the hydrogel coating layer 24, raising its temperature to about 60.degree.C and causing it to cure, i.e., to set up as a solid that is sufficiently stable to maintain its own shape and resist flow during storage or use. Once the heater 25 has warmed the hydrogel coating 24, it will be solidified and dimensionally stable. If curing is conducted without the application of heat, e.g., at room temperature, it will take longer than when heat is used. A liner sheet 26 such as polyethylene coated paper is then applied continuously by pressing it onto the exposed surface of the hydrogel layer 24 as the liner sheet 26 passes beneath a rotating roll 28. The assembled laminate 34 then moves further toward the right in the figure where a die press 30 stamps separate patches 32 from the sheet material.

The hydrogel 20, 24 comprises a hydrocolloidal dispersion of a hydrophilic natural or synthetic gel-forming polymer, a hydrophilic humectant, a biomedically active substance or medication, i.e., a medicament, and a hydrophilic **adhesive** substance such as an aqueous dispersion of an **acrylic adhesive**.

The polymer can comprise a natural **gum** such as **gum** karaya, **gum** acacia, locust bean **gum**, **guar gum**, or other polysaccharide as well as synthetically formulated polysaccharides, e.g., modified **guar gum**, maltodextrin, or celluloses such as carboxymethyl cellulose and carboxypropyl cellulose. The polymer can also comprise a synthetic polymer such as polyacrylamide and its congeners or polyacrylic acid. Polyacrylamide is sold under the trademark Polytec 31x by Tecna Corp., Belleville, New Jersey.

The humectant can comprise a polyhydric **alcohol** such as glycerol, propylene glycol, ethylene glycol, or sorbitol.

The **adhesive** can comprise any suitable biocompatible hydrophilic **adhesive** such as a resin emulsion **adhesive**, e.g., an **acrylate** emulsion **adhesive** or a copolymer of **vinyl** acetate and dioctyl maleate. The most outstanding results have been achieved with an **acrylic** emulsion **adhesive**. Other hydrophilic **adhesives** that can be used include an **acrylic** ester copolymer and a **vinyl** acetate resin.

Any of a variety of topical medications can be used in accordance with the present invention. The medications can be selected from a topical analgesic, anti-pruritic agent, anti-inflammatory agent, anesthetic agent, **keratolytic** agent and rubrefacient agent. When the patch is used as an analgesic, the analgesic can include trolamine salicylate, methyl salicylate, menthol, camphor, eucalyptus oil, spearmint oil, or a combination thereof. In other applications, the medication can include anti-pruritic agents or anti-inflammatory agent such as hydrocortisone, or anesthetic agents such as benzocaine or lidocaine. Also included are non-steroidal anti-inflammatory agents such as ibuprofen, especially the S-isomer of ibuprofen. Other medications that can be used include **keratolytic** agents such as **salicylic** acid, and rubrefacient agents such as capsicum.

In Fig. 2 the finished patch 32 is seen applied to the surface of the body with the backing 10 exposed and the pressure-sensitive hydrogel layer 24 bonded to the skin.

In Fig. 3 is shown a package containing the finished patch 32 as it appears during shipment and storage. The package 36 comprises a pouch including lower and upper layers of paper 35, 37 or other suitable packaging material such as metal foil coated paper which is sealed to itself along its edges, e.g., at 36a, 36b to provide a sealed pouch containing the finished patch 32.

As shown in Figs. 4 and 5, the finished patch 32 includes the porous backing 10, the hydrogel coating including the lower, i.e., external hydrogel coating layer 24 and the upper or internal portion 24a that permeates the backing 10. The upper surface 26a of the liner sheet 26 is a release surface for facilitating its removal. Before use, the liner sheet 26 is removed by pulling it off the patch as shown at the right in Fig. 4 to expose the pressure-sensitive surface of the layer 24 which is then applied to the skin as shown in Fig. 2.

During use, the upper or internal reservoir portion 24a that infiltrates the backing 10 and is solidified therein serves to store the medication within the backing 10 so that the medication migrates over time from its location at 24a within the backing 10 through the external coating layer 24 and then passes through the skin to provide sustained release of the medication into the body of the patient.

The porosity of the backing 10 combined with the water compatibility of the hydrocolloidal dispersion also makes the patch non-occlusive so that moisture from the body can evaporate through the patch into the atmosphere. The moisture vapor transmission rate (MVTR) of the skin alone under various conditions is typically from about 70 to about 149 g/m.²/24hr while the medication applying patch of the present invention is about 612 to 1952 g/m.²/24hr. This shows that the invention is non-occlusive because in a given period of time about 8 to 14 times more moisture vapor is transmitted through the patch of the present invention than through the skin. Prior medication-applying patches that employed a rubber backing allow virtually no moisture evaporation from the

skin. By contrast, the non-occlusive patch of the present invention will not interfere with moisture evaporation from the skin. This is important because the evaporation of moisture from the skin helps the skin to act in its normal capacity as a barrier to externally applied compounds which, if absorbed in excessive amounts, can produce toxic reactions or skin irritation. The invention thus enables the barrier function of the stratum corneum to be maintained.

When used as an analgesic patch, the present invention provides outstanding results in relieving pain such as arthritis pain and backache pain, as well as muscular aches and strains. Because of the thinness of the patch, it is perceived as being more comfortable, more flexible, less obtrusive and is more acceptable to the patient. The backing 10 is rendered so translucent by infiltration of the hydrocolloidal gel that the patch is very inconspicuous on the skin. The entire thickness of the analgesic patch is about 0.34 mm.

The invention will be better understood by reference to the following examples: <image> <image> <image> <image> <image>

Many variations of the present invention within the scope of the appended claims will be apparent to those skilled in the art once the principles described herein are understood.

CLAIMS (ENGLISH):

1. 2. The **adhesive** patch of claim 1 wherein the porous backing layer is a nonwoven fabric comprising water insoluble polymeric fibers with spaces therebetween.

2. 3. The **adhesive** patch of claim 2 wherein the nonwoven fabric comprises a mixture of polyester fibers and **cotton** fibers.

3. 4. The **adhesive** patch of claim 1 wherein the reservoir comprises a hydrocolloidal dispersion of a hydrophilic natural or synthetic gel-forming polymer, a liquid humectant, an **adhesive** with said biomedically active medication dispersed therein and the natural or synthetic gel-forming polymer comprises a member selected from the group consisting of **gum** karaya, **gum** acacia, locust bean **gum**, **guar gum**, modified **guar gum**, maltodextrin, carboxymethyl cellulose, carboxypropyl cellulose, polyacrylamide and its congeners, and polyacrylic acid.

4. 5. The **adhesive** patch of claim 1 wherein the reservoir contains a humectant which comprises a polyhydric **alcohol**.

5. 6. The **adhesive** patch of claim 5 wherein the polyhydric **alcohol** comprises a member selected from the group consisting of glycerol, propylene glycol, ethylene glycol, and sorbitol.

6. 7. The **adhesive** patch of claim 1 wherein the **adhesive** is a resin emulsion **adhesive**.

7. 8. The **adhesive** patch of claim 7 wherein the resin emulsion **adhesive** comprises a member selected from the group consisting of **acrylate** emulsion **adhesive**, an **acrylic** ester copolymer, a **vinyl** acetate resin, and copolymer of **vinyl** acetate and dioctyl maleate.

8. 9. The **adhesive** patch of claim 1 wherein the medication comprises one or more of the following: trolamine salicylate, methyl salicylate, menthol, camphor, eucalyptus oil, spearmint oil, hydrocortisone, benzocaine, lidocaine, ibuprofen, **salicylic** acid, and capsicum.

9. 10. The non-occlusive **adhesive** patch of claim 1 wherein the internal portion of the **adhesive** reservoir penetrates the porous backing layer to a depth of about at least one-fourth the thickness of the backing layer.

10. 11. The non-occlusive **adhesive** patch of claim 1 wherein the internal portion of the **adhesive** reservoir penetrates the porous backing layer to a depth of about nine-tenths the thickness of the backing layer.

11. 12. A method of forming a non-occlusive medication-containing **adhesive** patch to be applied to the skin for releasing a medication into the body of a patient comprising,
providing a porous backing layer of flexible water insoluble polymeric sheet material,
forming a dispersion of a polymer comprising an **adhesive** and a biomedically active medication to provide a pressure-sensitive hydrocolloidal gel reservoir,
expelling the hydrocolloidal gel onto the backing layer while maintaining the dispersion in a chilled condition,
the hydrocolloidal gel being chilled to a temperature effective to maintain the dispersion sufficiently fluid when applied to the backing layer to penetrate the backing layer to a depth of at least about one-fourth the thickness of the backing layer,
forming the hydrocolloidal gel into a coating on the backing, said coating having a flat, exposed, pressure-sensitive surface for bonding to the skin,
said pressure-sensitive hydrocolloidal gel reservoir thereby having two portions including:
(a) an external coating layer with said exposed surface for bonding to the skin, and
(b) an internal portion infiltrated within the pores of the backing layer, and allowing the hydrocolloidal gel to cure in place upon and within the porous backing layer.

12. 13. The method of claim 12 wherein the curing is accelerated by heating the hydrocolloidal gel after the gel has infiltrated into the pores of the backing layer.

13. 14. The method of claim 12 wherein the coating of the hydrocolloidal gel is formed by a knife coater to provide said pressure-sensitive surface for bonding to the skin.

14. 15. The method of claim 14 wherein a sheet of a liner paper is applied to the pressure-sensitive surface of the hydrocolloidal gel coating to protect the same during shipment and storage.

15. 16. The method of claim 12 wherein the dispersion is formed continuously within a processing mixer and is then applied as a continuous stream on a moving strip of said backing layer and a web of liner paper having a release surface is applied continuously to the exposed pressure-sensitive surface of the hydrocolloidal gel coating to protect the coating during shipment and storage, and said **adhesive** patches are cut therefrom.

16. 17. The method of claim 16 wherein the hydrocolloidal gel reservoir is infiltrated into the porous backing layer to a depth of between about one-fourth and nine-tenths the thickness of the backing layer and is solidified within the pores of the backing layer to unify the backing layer and the coating such that the backing layer acts as a storage location for the medication-containing hydrocolloidal gel reservoir.